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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,479	10/08/2003	Yin-Xiong Li	5405-295	7768
20792	7590	08/08/2006	EXAMINER	
MYERS BIGEL SIBLEY & SAJOVEC			STRZELECKA, TERESA E	
PO BOX 37428			ART UNIT	
RALEIGH, NC 27627			PAPER NUMBER	
			1637	

DATE MAILED: 08/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/681,479

Applicant(s)

LI ET AL.

Examiner

Teresa E. Strzelecka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 9 and 18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,6-8,10,11,16,17 and 19-24 is/are rejected.
- 7) ☒ Claim(s) 2-5 and 12-15 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. <u>7/17/06</u> . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>1/12/04;3/8/05</u> . | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

1. Applicants' election of Group I (claims 1-24) in the reply filed on May 30, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 813.03(a)).
2. Applicants cancelled claims 25-27, therefore only claims 1-24 are pending.
3. Claims 9 and 18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 30, 2006.
4. Claims 1-8, 10-17 and 19-24 will be examined.
5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

6. The information disclosure statements submitted January 12, 2004 and March 8, 2005 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Drawings

7. The drawings are objected to under 37 CFR 1.83(a) because they fail to show details in Figure 6, as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office

action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

8. Application record indicates that Applicants submitted color drawings or photographs on October 8, 2003. If applicants wish to have them published in color, please see 37 C.F.R. 1.84 for proper submission of color drawings/photographs.

Abstract

9. The abstract of the disclosure is objected to because it is longer than 150 words. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 is indefinite over the recitation of “wherein the first known segment and said second known segment comprise the same nucleic acid sequence in opposite orientation”. It is not clear what it means in terms of the sequence of the second known segment. If the first known segment is, in the 5’-3’ direction, 5’-AGCT-3’, does it mean that the second nucleic acid segment has a sequence 5’-TCGA-3’, or does it mean that it has the same sequence as the first one, but since it is ligated to the complementary strand it seems to be in “opposite” orientation.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 1, 6-8, 11, 16, 17 and 20-23 are rejected under 35 U.S.C 102(b) as anticipated by Zohlhofer et al. (WO 2001/71027) as evidenced by Eberwine et al. (PNAS USA, vol. 89, pp. 3010-3014, 1992).

Claims 1 and 11 will be considered together in claim 11, since it is a species of claim 1.

Regarding claims 1, 8 and 11, Zohlhofer et al. teach a method for amplifying mRNA, the method comprising:

(a) binding a first primer to a each of said target mRNA, the first primer comprising, in the 5' to 3' direction, a first known segment and an oligo T segment (page 1, first paragraph; page 7, last paragraph; page 8, first and second paragraphs.);

(b) transcribing a cDNA from said each of said target mRNA by elongation of said first primer with reverse transcriptase (page 1, first paragraph; page 5, second paragraph.); then

(c) linking a second known segment to the 3' terminus of each of said cDNAs (page 1, first paragraph; page 5, second paragraph; page 7, second and third paragraphs.); and then

(d) uniformly amplifying each of said cDNAs with a pair of primers, one of which pair binds to said first known segment and the other of which pair binds to said second known segment (page 1, first paragraph; page 5, second paragraph; page 30, last paragraph; page 31, first paragraph.).

Regarding claims 6 and 16, Zohlhofer et al. teach attachment of the tails using RNA ligase (page 1, first paragraph; page 5, second paragraph).

Regarding claims 7 and 17, Zohlhofer et al. teach segments comprising DNA (page 1, first paragraph; page 5, second paragraph; page 8, first and second paragraphs).

Regarding claim 20, Zohlhofer et al. teach mRNA extracted from a single cell or a few cells (page 10, second paragraph; page 29, first paragraph).

Regarding claim 21 and 23, Zohlhofer et al. teach amplification of mRNA from five cells (page 29, first paragraph). As evidenced by Eberwine et al., a single cell contains between 0.1 and 1 pg mRNA (page 3010, third paragraph), therefore by teaching five cells Zohlhofer et al. inherently teach no more than 10 nanograms of mRNA.

Regarding claim 22 and 23, Zohlhofer et al. teach quantitation of the amplified DNA (page 32, first paragraph).

14. Claims 1, 7, 8, 11, 17 and 20-23 are rejected under 35 U.S.C 102(e) as anticipated by Mueller et al. (U. S. Patent No. 6,558,927) as evidenced by Eberwine et al. (PNAS USA, vol. 89, pp. 3010-3014, 1992).

Claims 1 and 11 will be considered together in claim 11, since it is a species of claim 1.

Regarding claims 1 and 11, Mueller et al. teach a method for amplifying mRNA, the method comprising:

(a) binding a first primer to each of said target mRNA, the first primer comprising, in the 5' to 3' direction, a first known segment and an oligo T segment (Fig. 1; Fig. 2; col. 2, lines 52-60.);

(b) transcribing a cDNA from each of said target mRNA by elongation of said first primer with reverse transcriptase (Fig. 1; Fig. 2; col. 2, lines 52-60.); then

(c) linking a second known segment to the 3' terminus of each of said cDNAs (Fig. 1; Fig. 5; Fig. 6; col. 2, lines 61-67; col. 3, lines 1-29.); and then

(d) uniformly amplifying each of said cDNAs with a pair of primers, one of which pair binds to said first known segment and the other of which pair binds to said second known segment (Fig. 1; Fig. 8).).

Regarding claims 7 and 17 Mueller et al. teach DNA (col. 2, lines 52-60; col. 3, lines 5-12).

Regarding claim 8, Mueller et al. teach amplifying the cDNA with a pair of primers which bind to the first and second known sequences (Fig. 1 and 8).

Regarding claims 20 and 23, Mueller et al. teach 20 pg of mRNA (col. 7, lines 58, 59). As evidenced by Eberwine et al., a single cell contains between 0.1 and 1 pg mRNA (page 3010, third paragraph), therefore by teaching 20 pg of mRNA Mueller et al. inherently teach mRNA from fewer than 100 cells.

Regarding claim 21, Mueller et al. teach amplifying 2.5 ng, 0.5 ng, 100 pg and 20 pg of mRNA (col. 7, lines 58, 59).

Regarding claims 22 and 23, Mueller et al. teach quantitation of the mRNAs (Fig. 7).

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the

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subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

16. Claims 10, 19 and 24 are rejected under 35 U.S.C. 103(a) over Mueller et al. (U. S. Patent No. 6,558,927), Weissman et al. (U.S. Patent No. 6,235,502) and Lasken et al. (U.S. Patent No. 6,323,009).

A) The teachings of Mueller et al. are presented above. They teach amplification by PCR, but do not teach rolling circle amplification. They do not teach that the first and second known segments are the same.

B) Weissman et al. teach amplification of linear DNA sequences by rolling circle amplification by adding adapters with identical sequences to the ends of DNA and then amplifying the resulting circles with a single primer (Fig. 2; col. 4, lines 56-67; col. 5, lines 1-3).

C) Lasken et al. teach amplification of circular DNA targets using rolling circle amplification with multiple primers (Fig. 1; col. 3, lines 41-60; col. 4, lines 66, 67; col. 5, lines 1-11; col. 6, lines 50-67; col. 7, lines 1-21).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have converted the linear fragments of Mueller et al. into circles by the method of Weissman et al. which could be amplified by rolling circle amplification of Lasken et al. The motivation to do so, provided by Lasken et al., would have been that the amplification could be carried isothermally, was low cost, had high sensitivity and flexibility, and low risk of contamination (col. 2, lines 8-16) and allowed sequence determination from as little as 0.01 ng of circular template (col. 4, lines 51-57).

17. No references were found teaching or suggesting claims 2-5 and 12-15. Claims 2-5 and 12-15 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Teresa E Strzelecka
Primary Examiner
Art Unit 1637

Teresa Strzelecka
8/4/06